Attorney Docket No. VPI/02-115 US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application No.:	10/696,862
Confirmation No.:	8080
Filing Date:	October 30, 2003
Examiner:	Venkataraman Balasubramanian
Group Art Unit:	1624
Technology Center:	1600
Applicants:	Jingrong Cao et al.
For:	COMPOSITIONS USEFUL AS INHIBITORS OF ROCK AND OTHER PROTEIN KINASES

January 8, 2010
Cambridge, Massachusetts

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REPLY BRIEF UNDER 37 C.F.R. §41.41

Sir:

Applicants filed a Notice of Appeal on July 14, 2008 in the above-identified application and an Amended Appeal Brief on September 10, 2009. On December 9, 2009, an Examiner's Answer to the Amended Reply Brief was mailed. This Reply Brief is responsive to the Examiner's Answer. Since 37 C.F.R. §41.41 sets a two-month time period for reply based on the mailing date of the Examiner's Answer, this Reply is timely submitted.

Appellants' argument begins on page 2 of this Reply Brief.

REPLY ARGUMENT

On page 11 of the Examiner's Answer, the Examiner asserts that appellants' assessment of the biological data is not entirely correct and accurate. The Examiner further asserts that there is no clear-cut definition of what is inferior as relates to biological data. In addition, the Examiner states that there is nothing in Japanese Patent Application No. 2002053566 (hereafter, "Inaba") which indicates or states the pyridinyl thiazoles are not suitable for the use taught therein that would deter one away from making these compounds. The Examiner's contention is as follows:

> The biological activity shown in pages 185-196 are activity among three isoforms of PKC and most [of] them [fall far] below < 1 micromolar for at least one isoform and ***on the whole*** are well below 5 micromolar. [emphasis added]

First, the Examiner's use of IC_{50} data in his argument indicates that there is a clear-cut definition for what is inferior. That is, a person skilled in the art would recognize that compounds with higher IC_{50} values are inferior to those with lower IC_{50} values, just as the Examiner has so argued. More importantly, the Examiner fails to appreciate the kernel of appellants' argument, which is that it is not the activity of the Inaba compounds *as a whole* that is important in the determination of obviousness. Rather, it is whether one skilled in the art would have chosen either cited compound 44 or compound 113 as a lead compound worthy of further investigation.

As applicants have correctly stated, compound 44 is an inferior kinase inhibitor when compared to the vast majority (90%) of the other compounds of Inaba for which similar data are reported. Further, it is a relatively poor kinase inhibitor when compared with the best compounds of Inaba. This is also true of compound 113. See Table 1, which provides IC_{50} values for compounds 44 and 113 and compares these values with the IC_{50} values of the most active compounds for which biological data were reported.

Table 1. Comparative activities of Compounds 44 and 113

	PKC-α (IC_{50} μM)	PKC-β (IC_{50} μM)	PKC-γ (IC_{50} μM)
Compound 44	4.2445	18.6092*	0.505
Compound 113	0.1352	0.4307	0.2066
Most active compounds of Inaba	0.01 (compound 109)	0.0253 (compound 109)	0.0115 (compound 170)

* Note: In his Answer, the Examiner incorrectly stated that compound 44 had an activity of < 1 μM for the inhibition of PKC-β.

As indicated in the table, the best compounds of Inaba are at least an order of magnitude more potent that either compound 44 or compound 113. Accordingly, based on the teachings of Inaba, a skilled person would not consider either of these two compounds, or compounds closely related to them, as a lead compound when formulating a strategy to prepare efficacious pharmaceuticals.

Respectfully submitted,

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